

What is claimed is:

1. A composition comprising complementary fragments of a protein, said fragments
5 generating an optically detectable signal when associated.
2. The composition of claim 1 wherein said fragments generate a fluorescent signal when
associated.
- 10 3. The composition of claim 1 wherein said fragments generate a luminescent signal
when associated.
4. The composition of claim 1 wherein said fragments generate a phosphorescent signal
when associated.
- 15 5. The composition of claim 1 wherein said fragments are derived from a fluorescent
protein.
6. The composition of claim 5 wherein said fragments are derived from a mutant
20 fluorescent protein.
7. The composition of claim 6 wherein said complementary fragments differ from the
corresponding fragments of the wild-type protein by at least one amino acid.

8. The composition of claim 6 wherein said complementary fragments are selected from the group consisting of: Seq. ID NO: 20 to Seq. ID NO: 1067.

9. The composition of claim 8 wherein said Seq. ID NO: 20 to Seq. ID NO: 1067 are
5 further fused to a separate molecule.

10. A composition comprising complementary fragments of a mutant protein, said fragments generating an optically detectable signal when associated, wherein each fragment is fused to a separate molecule.
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11. The composition of claim 10 wherein said fragments generate a fluorescent, luminescent or phosphorescent signal when associated.

12. The composition of claim 10 wherein said complementary fragments differ from the
15 corresponding fragments of the wild-type protein by at least one amino acid.

13. Protein fragment complementation assays for the detection of molecular interactions comprising a reassembly of separate fragments from an optically detectable protein wherein reassembly of the fragments is operated by the interaction of molecular domains fused to each
20 fragment, wherein reassembly of the fragments is independent of other molecular processes and wherein said reassembly is detected by means of reconstitution of activity of said optically detectable protein.

14. The assays of claim 13 wherein said fragments generate a fluorescent signal when associated.

15. The assays of claim 13 wherein said fragments are derived from a mutant fluorescent
5 protein.

16. A method for detecting biomolecular interactions said method comprising:

- (a) selecting an appropriate optically detectable protein;
- (b) effecting fragmentation of said optically detectable protein such that said
10 fragmentation results in reversible loss of protein function;
- (c) fusing or attaching fragments of said optically detectable protein separately to other molecules;
- (d) reassociating said protein fragments through interactions of the molecules that are fused or attached to said fragments; and
- 15 (e) detecting the resulting optical signal.

17. The method of claim 16 wherein said optically detectable reporter protein is a mutant fluorescent protein.

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